DYNE-401 demonstrates potential to deliver functional improvement in Pompe disease with low and infrequent dosing[1]

Tyler Picariello, Ph.D.

Dyne therapeutics, Inc.

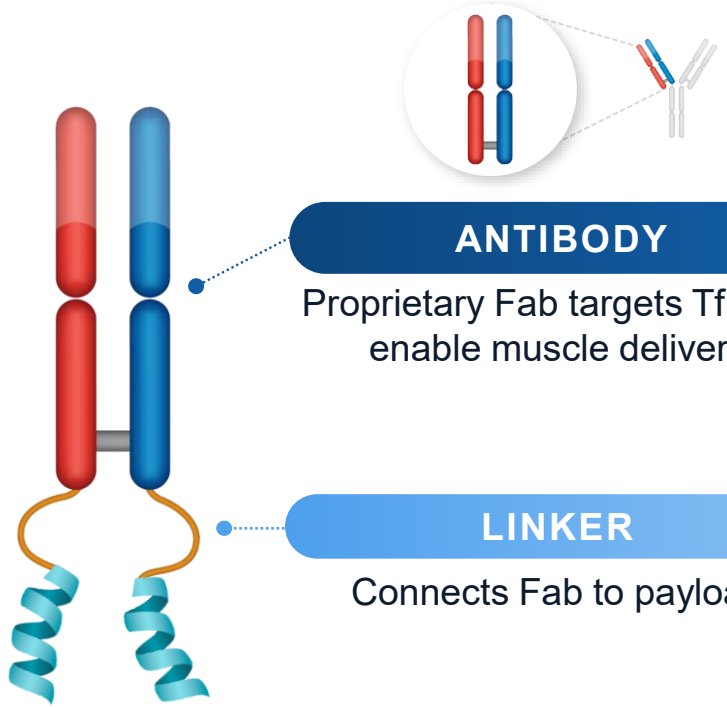
[1] Previously presented: Picariello, T. et al., (2026) *Molecular Genetics and Metabolism*, 147;(2).

MDA Clinical & Scientific Conference March 8-11, 2026

Disclosures

I Tyler Picariello am an employee of Dyne Therapeutics, Inc.

Dyne FORCE platform modularity enables diversified pipeline to address DM1, DMD, FSHD, and Pompe disease



ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery

LINKER

Connects Fab to payload

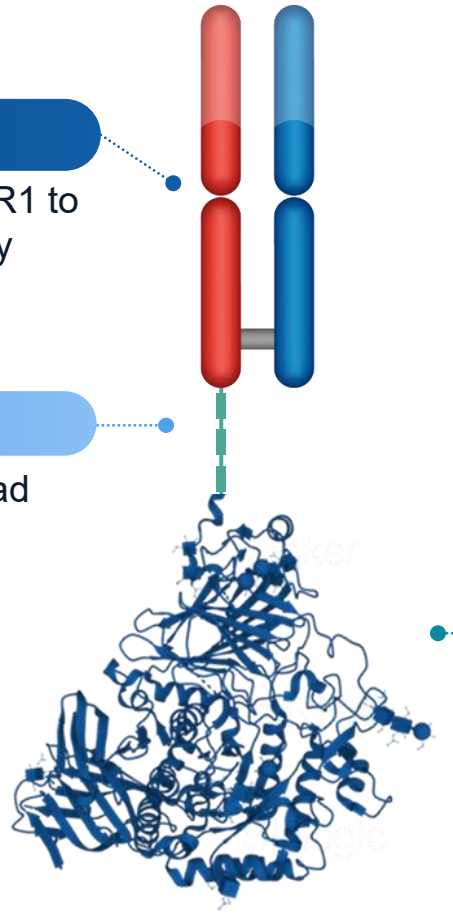
OLIGO PAYLOAD

Rationally selected to target the genetic basis of disease

Gapmer ASO for *DMPK* KD: DM1

PMO for exon 51 skipping: DMD

siRNA for *DUX4* KD: FSHD



BIOLOGIC PAYLOAD

Notes: The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Pompe disease is a rare and serious neuromuscular lysosomal storage disorder (LSD)

~4,500 patients in US

Low GAA activity leads to lysosomal glycogen accumulation

Infantile-onset (IOPD; 10% of population)

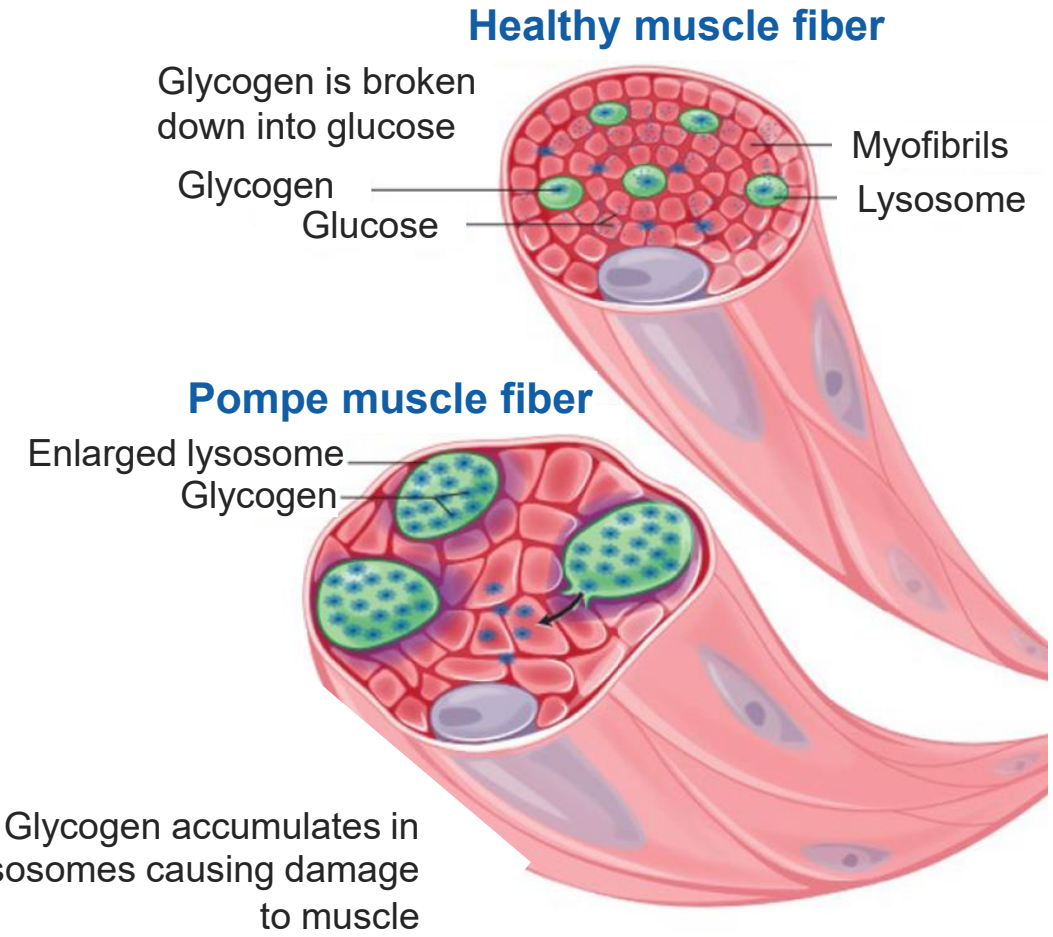
- Cardiomyopathy and cardiomegaly
- Progressive muscle weakness and respiratory failure
- CNS manifestations including decreased IQ

Late-onset (LOPD; 90% of population)

- Progressive muscle weakness with mobility issues
- Respiratory insufficiency

Therapeutic modalities:

- ERT with GAA
- SRT with *GYS1* siRNA
- Gene therapy



Notes: SRT = substrate reduction therapy; NINDS; Lim, J-A. et al., 2014; Van der Ploeg, A.T. and Reuser, A.J., 2008; Fusco, A.F., et al., 2020; van der Beek, N.AME., et al. 2012; Rabin, N., et al., 2003; Image from: Pompe Disease Family Education booklet University of Michigan Medicine, CC; BY-SA 4.0 https://www.med.umich.edu/1libr/Pediatrics/Genetics/PompeDiseaseBooklet.pdf

Leveraging FORCE to improve efficacy of ERT in Pompe disease

DYNE-401 enables TfR1-targeted ERT

Antibody

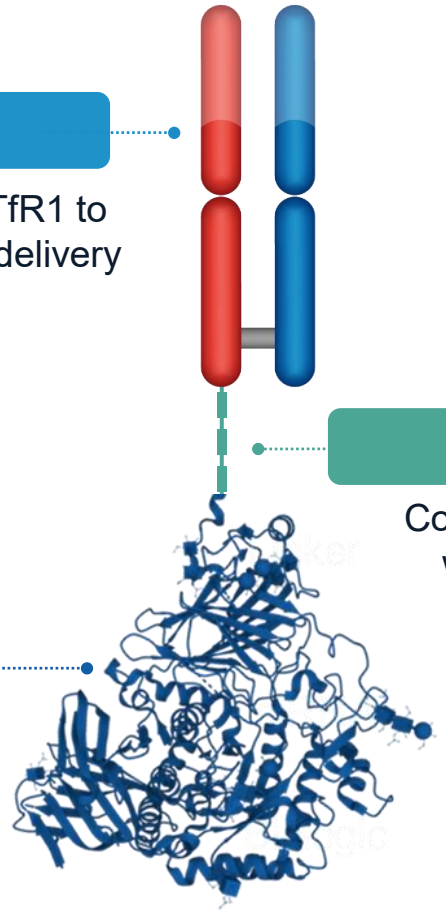
Proprietary Fab targets TfR1 to enable muscle and CNS delivery

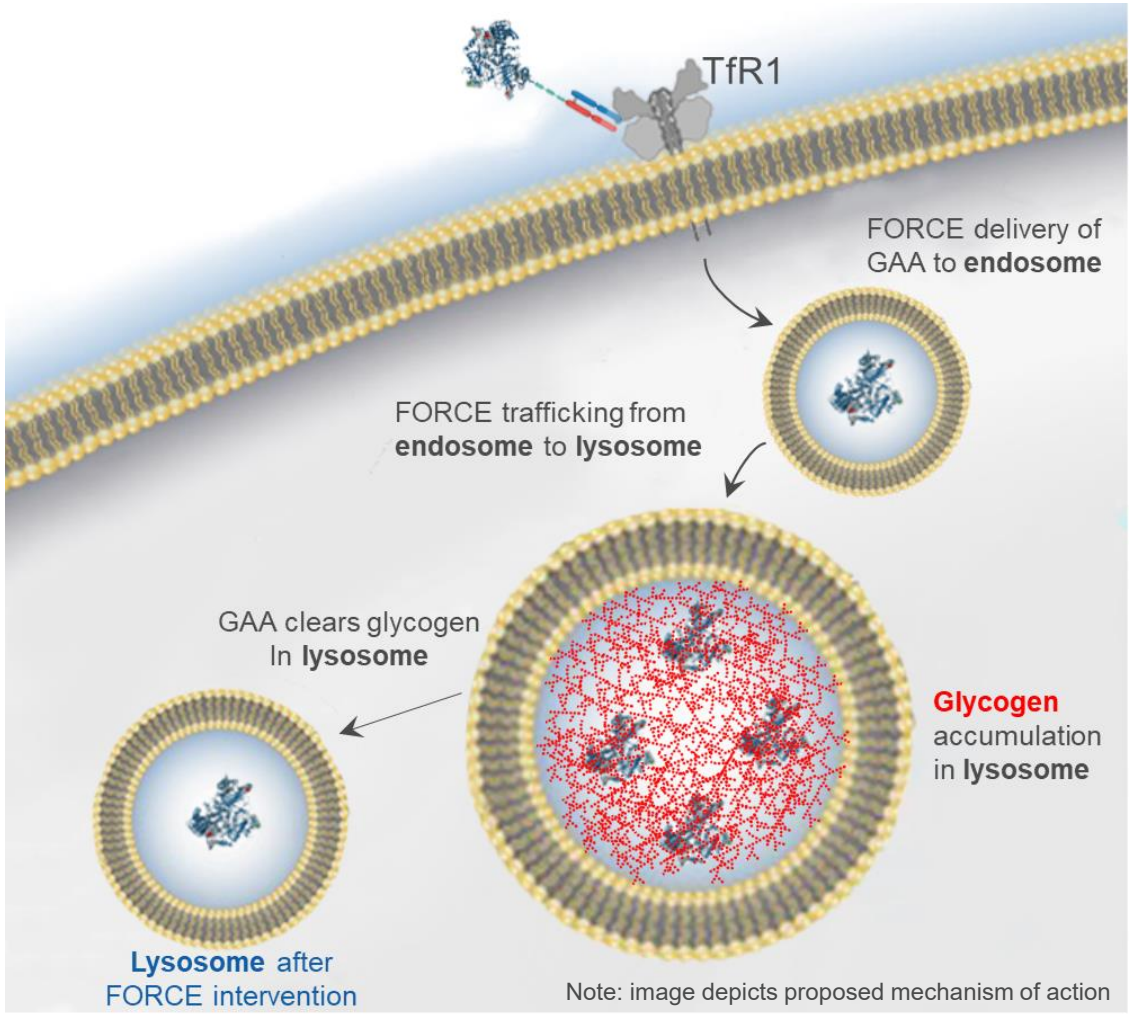
Linker

Connects Fab with GAA

Payload

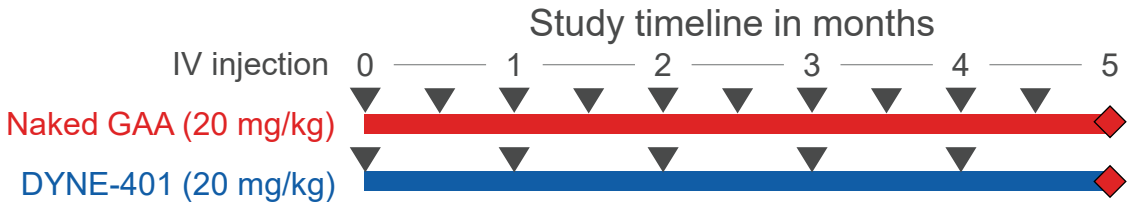
GAA to address Pompe pathology





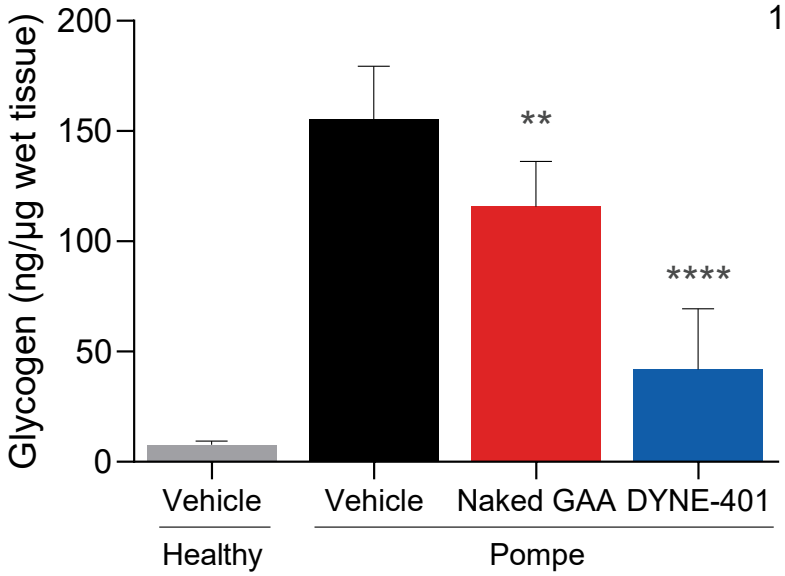
The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Monthly DYNE-401 is superior to naked GAA and sustains functional improvement in Pompe disease mice

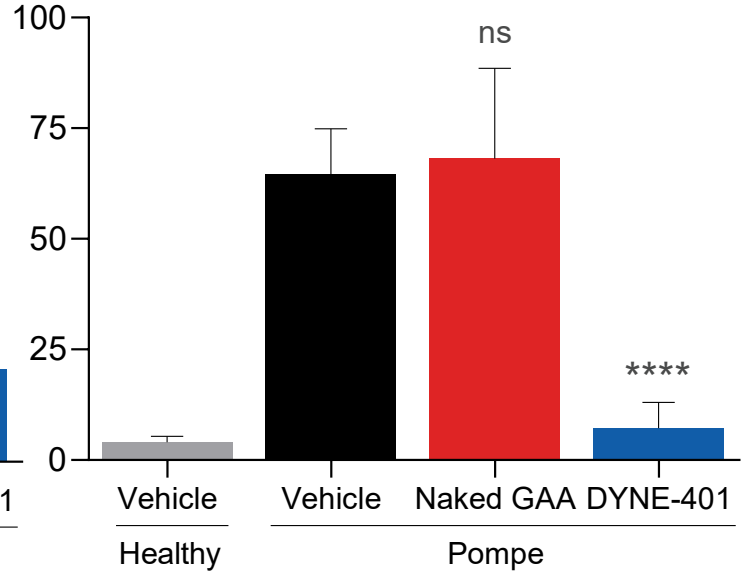


Glycogen reduction

Tibialis anterior

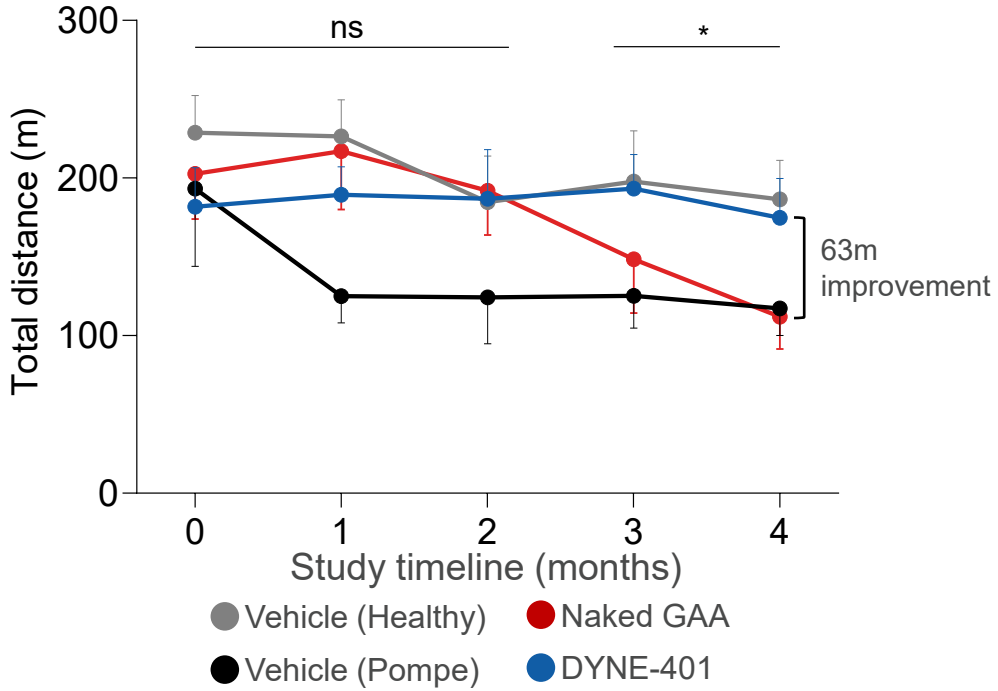


Cerebral cortex



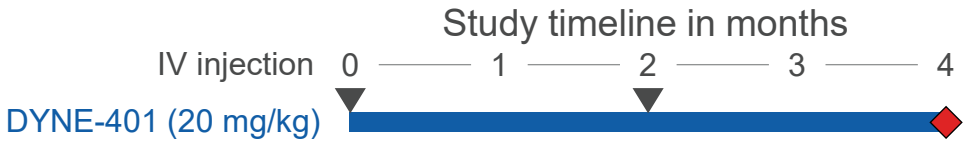
Functional improvement

Running distance

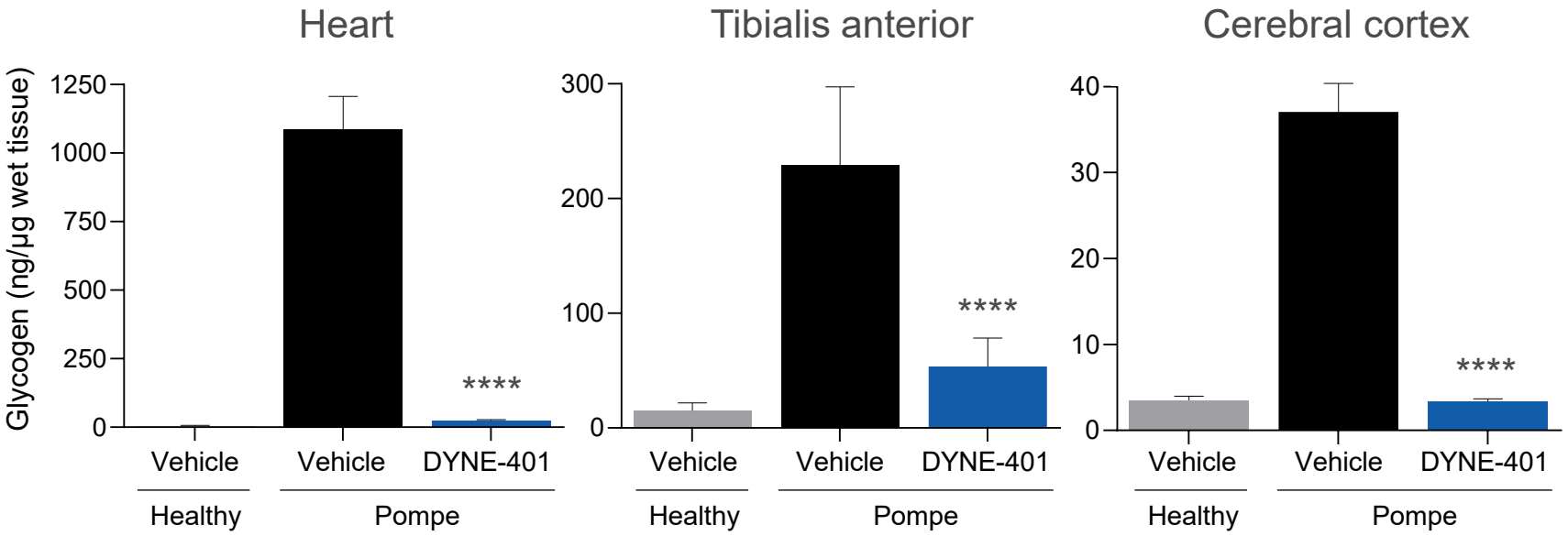


Notes: Mice were dosed with naked GAA every other week or DYNE-401 every month for the duration of the study. Mice were necropsied five months after study start. Doses are mg/kg GAA-equivalents. Healthy mice are hTfR1$^{hu/mu}$;Gaa$^{WT/Neo}$; Pompe mice are hTfR1$^{hu/mu}$;Gaa$^{Neo/Neo}$ mice. N=7-9 mice per group; data are mean ± SD; Data analyzed by one-way ANOVA followed by Turkey's test; ** = *p≤0.01;* **** *p ≤ 0.0001.* The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

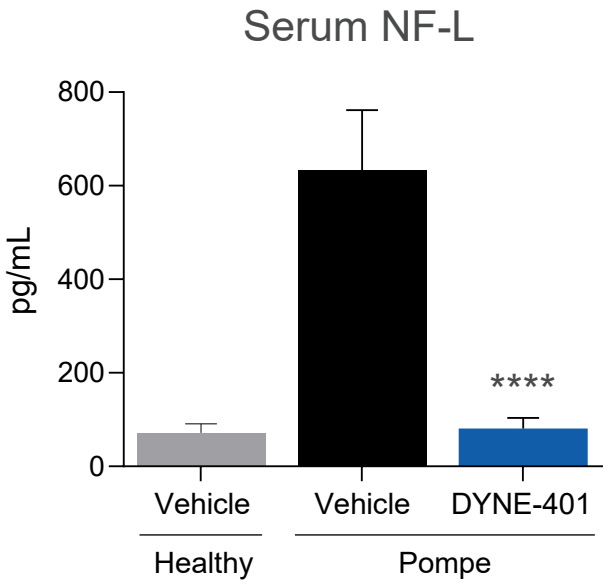
DYNE-401 demonstrates potential for every other month dosing



DYNE-401 clears glycogen in muscle and CNS

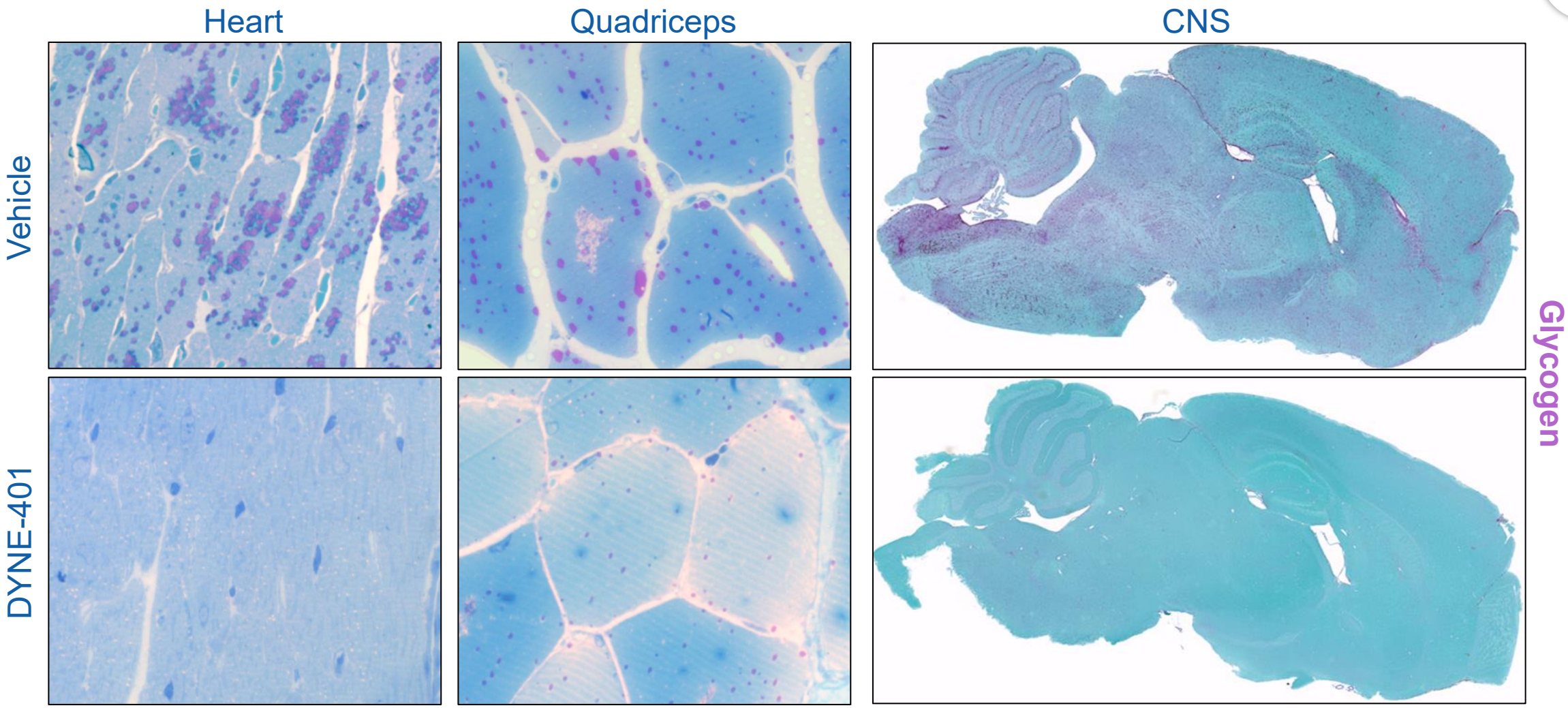


DYNE-401 reduces serum NF-L, a biomarker of axon damage



Notes: Mice we dosed with DYNE-401 at study start and at month two. Mice were necropsied four months after study start. Doses are mg/kg GAA-equivalents. Healthy mice are hTfR1$^{hu/mu}$;Gaa$^{WT/Neo}$; Pompe mice are hTfR1$^{hu/mu}$;Gaa$^{Neo/Neo}$ mice. N=4-5 mice per group; data are mean ± SD; statistical significance determined by One-way ANOVA with Turkey's multiple comparisons test; *=$p<0.05$; ** = $p<0.01$; **** $p<0.0001$; The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

DYNE-401 achieves uniform glycogen clearance in muscle and CNS with every other month dosing



Notes: : Mice we dosed with DYNE-401 at study start and at month two. Necropsy occurred at month four. Muscle sections were processed in Epon-Araldite resin. Brains were formalin fixed and paraffin embedded. The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Conclusions

- DYNE-401 demonstrates superior efficacy in muscle compared to naked GAA in a well-established mouse model of Pompe disease
- DYNE-401 addresses CNS pathology in Pompe mice
- DYNE-401 has the potential to deliver functional improvement in Pompe disease with infrequent dosing
- FORCE is a modular drug delivery platform that enables muscle and CNS distribution of biologics as well as oligonucleotide payloads

Notes: The FORCE platform and FORCE-GAA are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Acknowledgements

Dyne Research and Development

Special thanks

- Beth Thurberg
- Nancy Andrews